

Umbilical cord lactate compared with pH as predictors of intrapartum asphyxia

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Abstract. Despite advances in fetal monitoring during labor, one of the most critical causes of neonatal death and neurologic injuries remains intrapartum asphyxia. Umbilical cord gases can be used to detect acidosis and fetal distress. We conducted a retrospective, multicenter study to evaluate umbilical cord blood pH and lactate as a mean of evaluating the degree of intrapartum hypoxia and also to establish which of the two is more reliable in predicting morbidity in term neonates. The present study utilized a total of 124 cases that met the criteria for intrapartum asphyxia and 150 normal term newborns that were randomly selected as case control. Both umbilical cord lactate and pH proved to be accurate predictors of neonatal morbidity caused by intrapartum hypoxia. Lactate proved to be superior to pH in predicting adverse neonatal outcome. The

greatest sensibility and specificity in predicting intrapartum asphyxia were achieved in our study by using a cutoff value of 3.75 mmol/l for lactate and 7.24 for pH.

Introduction

Despite the advances in fetal monitoring during labor, one of the most critical causes of neonatal death and neurologic injuries remains intrapartum asphyxia (IA) (1-4). During labor and birth, IA leads to hypoxia and fetal acidosis. Thus, a reliable method for detecting acidosis can be a useful tool for predicting adverse neonatal outcome due to IA (2,5-7).

Acidosis can be evaluated and it is defined as low umbilical cord pH or high umbilical base deficit (expressed as negative base excess, BE) at birth (7-9). Hypoxia due to impaired blood supply to the fetus leads in the early stages to respiratory acidosis that is characterized by a decrease in pH but normal BE. Following these initial events, if hypoxia continues there will be a shift to anaerobic metabolism, resulting in the formation of lactic acid and increase in BE (6,8,9). Thus, high cord blood lactate levels can be correlated with fetal acidosis and asphyxia (10,11).

Some studies suggest that neonatal complications are associated with metabolic acidosis, rather than respiratory acidosis, thus a distinction between the two is important for predicting those neonate at risk for morbidity and mortality (6,12). Because lactate is a direct end product of anaerobic metabolism it can be used to differentiate between metabolic and respiratory acidosis. Furthermore, some studies suggest that the measurement of umbilical cord blood lactate is more accurate

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than pH measurements in predicting neonatal outcome (10,13). Since labor and birth can be complicated by a wide variety of events such as retroplacental hematoma, prematurity, and dystocia, it is important to be able to objectively confirm or infirm intrapartum hypoxia (12-14).

Perinatal hypoxia is difficult to predict and avoid, as it can be the result of fetal malformations, prematurity, labor dystocia or unexpected events such as retroplacental hematoma (14,15). In addition, in some cases even less severe pathologies such as thrombophilia can be an important risk factor for perinatal hypoxic events (16-18). Thus, an objective mean of assessing fetal hypoxia is important for confirming or excluding intrapartum asphyxia and predicting neonatal long term morbidity and mortality (19,20).

We conducted a retrospective, multicenter study to evaluate umbilical cord blood pH and lactate as a mean of evaluating the degree of intrapartum hypoxia and also to establish which of the two is more reliable in predicting morbidity in term neonates. This study continues and extends the research previously carried out by Mogos *et al* at a single center (7).

Patients and methods

Newborns. Our study included newborns born between 2010 and 2012 in three hospitals in Romania: INSMC 'Alessandrescu Rusescu', Bucur Maternity Hospital and Craiova Emergency Hospital. The information was gathered from the archived patient medical records and included gestation age, fetal heart rate monitoring during labor, birth weight, Apgar score, umbilical blood gases (pH and lactate) and neonatal outcome. The data collected retrospectively did not contain personal information and only the agreements of the ethics committee of the participant hospitals were required and obtained without the need of informed consent or the consent of the patient/legal representative in the case of minors.

We included in the intrapartum asphyxia group (IA) all newborns from term singleton births with markers of a severe hypoxic event during labor defined as the presence of at least one of the following: Severe changes in fetal heart rate (<100, >160), meconium staining and in the presence of at least one of the following: Low Apgar score (≤ 3 in the first minute or ≤ 5 after 5 min); respiratory failure (defined/characterized as absence of spontaneous breathing after more than 5 min or mechanical ventilation for more than 10 min); the need for intensive care unit admission for more than 24 h.

The exclusion criteria for the IA group were: Encephalopathy determined by causes other than IA, congenital malformations, congenital metabolic diseases, viral infection, septic shock, major organ failure, or fetal trauma during birth.

A control group of 150 healthy newborns from term singleton births, that did not meet any of the above criteria (IA or exclusion), and that had information regarding umbilical cord gases, was randomly selected from the newborn that were registered between 2010 and 2012.

Term pregnancy was defined as a gestational age of 37 weeks or greater and only singleton pregnancies were selected.

Receiver operating characteristics (ROC) curves were constructed to evaluate the predictive value of pH and lactate for fetal asphyxia and neonatal death. To objectively compare

Table I. pH and lactate values in the IA and control groups.

Variable	IA group (n=124)	Control group (n=150)
pH	7.17 \pm 0.07 (7.05-7.32)	7.28 \pm 0.06 (7.13-7.38)
Lactate (mmol/l)	5.34 \pm 1.5 (2.35-8.75)	2.78 \pm 0.7 (1.25-4.35)

Data are expressed as mean \pm SD (range). P<0.001, IA group compared with the control group. IA, intrapartum asphyxia.

the predictive characteristic of pH and lactate we used the maximal Youden index to determine the 'optimal' cutoff value for each variable. The Youden index takes into account sensitivity and specificity and it is used to estimate the diagnostic effectiveness of different cutoff values (19).

Statistical analysis. The data were collected using Office-Excel version 14.7.7 and for the statistical analysis NCSS 2019 Statistical Software (2019) (NCSS, LLC.; ncss.com/software/ncss) was used. The characteristics for each group were calculated using 'Descriptive statistics'. The variables were compared using two sample t-test. The results were analyzed and interpreted according to the obtained P-value; P<0.05 was considered to be statistically significant.

Results and discussion

During the period 2010-2012 there were 21,224 births; a total of 124 cases met our criteria for IA. The umbilical cord pH was significantly lower (P<0.001) in the IA group, with a mean of 7.17 with values ranging between 7.05 and 7.32, compared to a mean of 7.28 for the Control group (Table I, Fig. 1). In addition, the lactate values were significantly higher (P<0.001) for the IA group, with a mean of 5.34 mmol/l and values ranging between 2.35 and 8.75 mmol/l, compared to a mean of 2.78 mmol/l for the Control group (Table I, Fig. 1).

The ROC curves for lactate and pH for evaluating IA are shown in Fig. 2. The pH had a ROC curve area of 0.75, while the lactate had a ROC curve area of 0.92; thus, lactate was significantly more accurate in predicting IA. Judging by the maxim Youden index, the optimal cutoff value was 7.24 for pH with an index of 0.62 and 3.75 mmol/l for lactate with an index of 0.70 (Table II). Both sensitivity and specificity were higher for lactate compared to pH (87.1 and 83.2% compared to 86.3 and 74.0%).

Umbilical cord gases represent one of the most objective ways to evaluate newborn metabolic status and rule out perinatal asphyxia (21,22). In our study, the results confirm that increased umbilical cord blood lactate is an accurate predictor of neonatal morbidity due to intrapartum asphyxia. By comparing the ROC curve areas, lactate proved to be superior to pH in predicting poor neonatal outcome. In addition, although there are numerous proposals for cutoff values of pH and lactate to be used for confirming IA and predicting a poor outcome (23,24), the greatest sensitivity and specificity were achieved in our study by using a cutoff value of 7.24 for pH and 3.75 mmol/l for lactate (Table II).

There are two possible explanations for which lactate appears to be superior in predicting neonatal morbidity and

Table II. Sensitivity and specificity of the different cutoff values for pH and lactate for evaluating IA.

Variable	Sensitivity (95% CI)	Specificity (95% CI)
pH		
≤7.12 (10th percentile)	31.4% (23.4-40.4)	99.9% (97.5-100)
≤7.17 (mean IA value)	50.8% (41.6-59.8)	93.3% (88.1-96.7)
≤7.24 ('optimal cutoff' from the ROC curve)	86.3% (78.9-91.8)	74.0% (66.2-80.8)
Lactate (mmol/l)		
≥7.00 (90th percentile)	27.4% (19.7-36.1)	99.9% (97.5-100)
≥5.35 (mean IA value)	48.4% (39.3-57.5)	98.6% (95.2-99.8)
≥3.75 'optimal cutoff' from the ROC curve	87.1% (79.8-92.4)	83.2% (76.3-87.5)

IA, intrapartum asphyxia; CI, confidence interval; ROC, receiver operating characteristics.

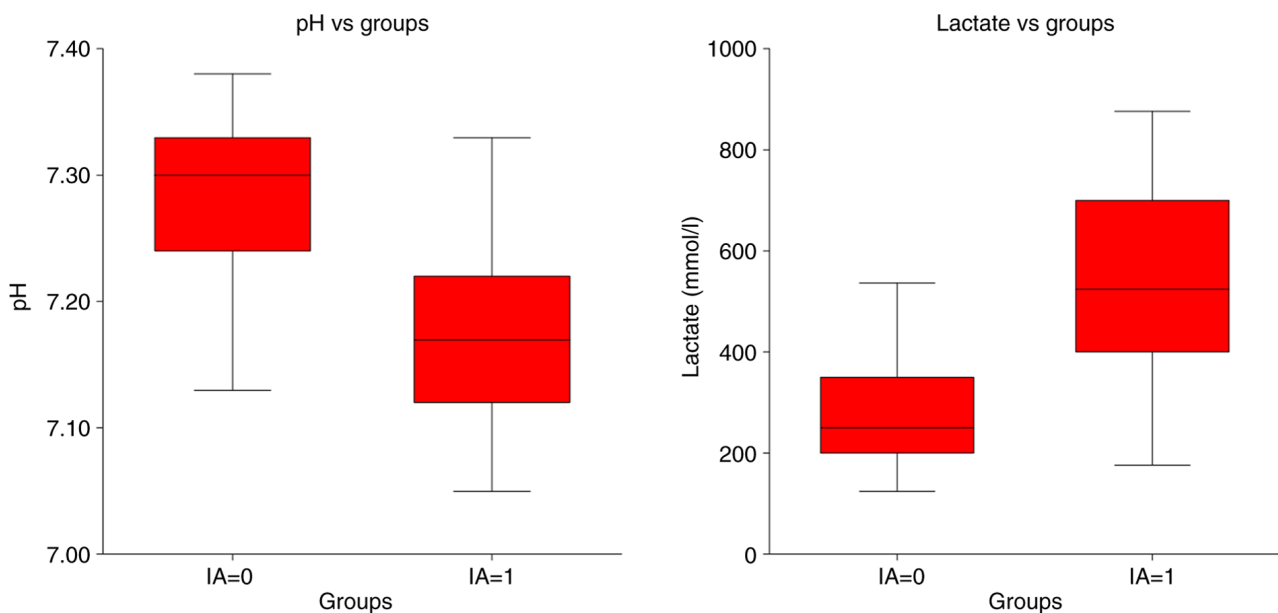


Figure 1. Box plots for pH and lactate values in the IA and Control groups. IA=1, control group; IA=1, IA group; IA, intrapartum asphyxia.

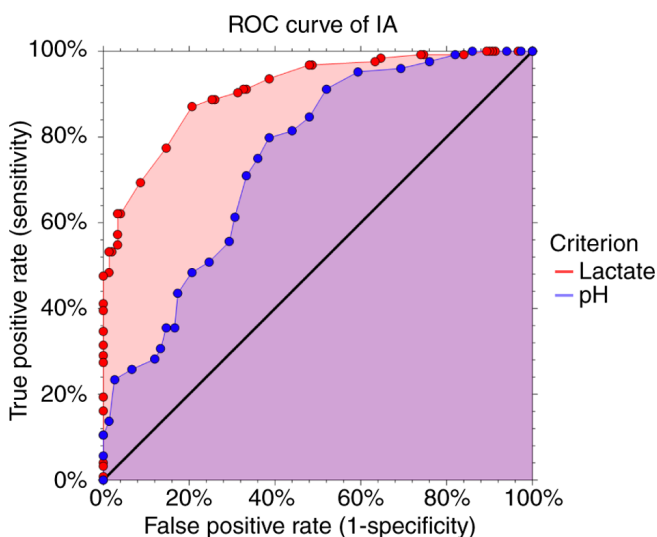


Figure 2. Receiver operating characteristic (ROC) curves of pH and lactate for the diagnosis of IA. IA, intrapartum asphyxia.

mortality. First of all, lactate is a direct product of anaerobic metabolism; thus, it is produced earlier during hypoxia. Therefore, changes in its value occur and can be detected more rapidly than low pH (25,26). Secondly, high umbilical cord blood lactate is a specific marker of metabolic acidosis which is associated with more neonatal complications than respiratory acidosis (6,12).

As with premature births, we are still far from being able to predict and avoid intrapartum asphyxia, despite the efforts made over the last decades (27). As technology progresses, probably more and more sensors and intelligent textiles will be developed, that will be able to detect fetal hypoxia and distress before severe lesions occur. Yet, until that time, evaluating cord blood gases remains one of the most reliable ways of detecting but also excluding fetal hypoxia (20,28,29). Moreover, in today's era of defensive medicine and prenatal diagnostics, it is important to rule out IA as a contributing cause for the poor neurological outcome of neonates diagnosed prenatally with complex malformations such

as holoprosencephaly, Galen vein aneurism or other brain anomalies (30-35).

In 2014, the American College of Obstetricians and Gynecologists compiled a summary of all specified signs present in the neonatal period and all the factors that suggest or lead to a diagnosis as early as possible of an acute perinatal hypoxic-ischemic event (36). The first neonatal sign is an Apgar score below 5 at 5 and 10 min, which then is followed by fetal acidemia in the umbilical artery with a pH <7.0 or the presence of base deficit ≥ 12 mmol/l, separately or together. Furthermore, the impact of IA can be observed by imaging through magnetic resonance imaging or spectroscopy where acute brain injuries can be noted (37,38). The next sign of certainty is the presence of hypoxic-ischemic encephalopathy and multisystem organ failure. Early detection of these signs may limit the progression to irreversible consequences (39).

One limitation of our study was that it included only term neonates thus the results may not be valid for preterm births. Moreover, only short-term outcome was taken into consideration. Thus, future studies may be needed to assess the predictive ability of pH and lactate for long-term outcomes and in cases of premature birth.

In conclusion, both umbilical cord lactate and pH can be used as accurate predictors of neonatal morbidity caused by intrapartum hypoxia, as it has been showed in numerous studies. Our study confirmed that lactate is superior to pH in predicting adverse neonatal outcome. The greatest sensitivity and specificity in predicting IA were achieved in our study by using a cutoff value of 3.75 mmol/l for lactate and 7.24 for pH. For these cutoff values, the sensitivity and specificity for lactate were 87.1 and 83.2%, while for pH they were 86.3 and 74.0%.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

AN, REB and CGH collected, analyzed and interpreted the patient data. SV, MCTD and LP collected the data and had substantial contribution to the conception of the research and statistical analysis. ADB, LN and NB substantially contributed to the conception of the study, the interpretation of the data and the writing of the manuscript. LIC and RGI contributed to the literature retrieval and manuscript modification. AN, REB and FF supervised and designed the present study and contributed to the approval of the final version of the manuscript. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

The data collected retrospectively did not contain personal information and only the agreement of the ethics committee of INSMC 'Alessandrescu Rusescu' Bucharest, Bucur Maternity Hospital Bucharest and Craiova Emergency Hospital were required and obtained without the need of informed consent or the consent of the patient/legal representative in the case of minors.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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